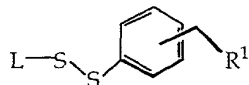


IT IS CLAIMED:

1. A conjugate for use in a liposomal drug-delivery vehicle, the conjugate having the general structural formula:

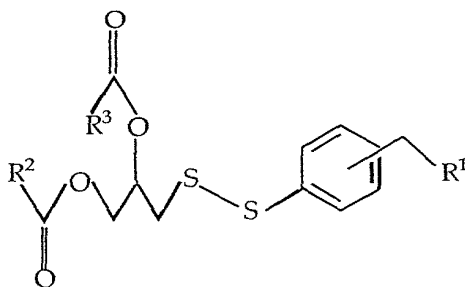


wherein L is a hydrophobic moiety suitable for incorporation into a liposomal lipid bilayer,  $\text{R}^1$  represents a therapeutic drug covalently attached to the dithiobenzyl moiety, and where orientation of the  $\text{CH}_2\text{R}^1$  group is selected from the ortho position and the para position.

2. The conjugate of claim 1, wherein the therapeutic drug is covalently attached by a linkage selected from the group consisting of urethane, amine, amide, carbonate, thio-carbonate, ether and ester.

3. The conjugate of claim 1, wherein L is selected from the group consisting of cholesterol, a diacylglycerol, a phospholipid and derivatives thereof.

4. The conjugate of claim 1, wherein L is a diacylglycerol derivative to yield a conjugate having the general structural formula:



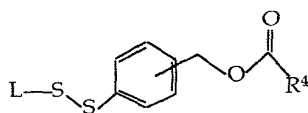
wherein  $\text{R}^2$  and  $\text{R}^3$  are hydrocarbons having between about 8 to about 24 carbon atoms.

5. The conjugate of claim 4, wherein  $R^2$  and  $R^3$  are hydrocarbons having from about 12 to about 22 carbon atoms.

6. The conjugate of claim 4, wherein  $R^2$  and  $R^3$  are hydrocarbon chains of the same length.

7. The conjugate of claim 1, wherein said drug is selected from the group consisting of mitomycin C, mitomycin A, bleomycin, doxorubicin, daunorubicin, fluorodeoxyuridine, iododeoxyuridine, etoposide, AZT, acyclovir, vidarabine, arabinosyl cytosine, pentostatin, quinidine, atropine, chlorambucil, methotrexate, mitoxantrone and 5-fluorouracil.

8. The conjugate of claim 1, wherein the therapeutic drug is covalently linked to the dithiobenzyl moiety to form a conjugate having the structure:



wherein  $R^4$  represents a residue of the therapeutic drug.

9. The conjugate of claim 8, wherein  $R^4$  is a therapeutic drug residue containing a primary or a secondary amine moiety thereby forming a urethane linkage between the dithiobenzyl and the therapeutic drug.

10. The conjugate of claim 9, wherein said therapeutic drug is selected from the group consisting of mitomycin A, mitomycin C, bleomycin and a polypeptide.

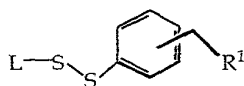
11. The conjugate of claim 8, wherein  $R^4$  is a residue of a carboxyl-containing therapeutic drug, thereby to form an ester linkage between the dithiobenzyl and the therapeutic drug.

12. The conjugate of claim 11, wherein said drug is chlorambucil or methotrexate.

13. The conjugate of claim 8, wherein R<sup>4</sup> is a therapeutic drug residue containing a hydroxyl moiety thereby to form a carbonate linkage between the dithiobenzyl and the therapeutic drug.

14. The conjugate of claim 13, wherein the therapeutic drug is selected from the group consisting of fluorodeoxyuridine, iododeoxyuridine, etoposide, AZT, acyclovir, vidarabine, arabinosyl cytosine, pentostatin, quinidine, mitoxantrone and atropine.

15. A liposome composition, comprising liposomes comprised of vesicle-forming lipids including from about 1 to about 30 mole percent of a conjugate having the general structural formula:



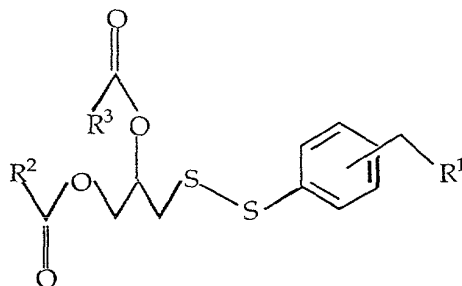
wherein L is a hydrophobic moiety suitable for incorporation into a liposomal lipid bilayer, R<sup>1</sup> represents a therapeutic drug covalently attached to the dithiobenzyl moiety, and where orientation of the CH<sub>2</sub>R<sup>1</sup> group is selected from the ortho position and the para position,

wherein said therapeutic drug is released from the conjugate in vivo in response to a physiologic condition or an artificially induced condition.

16. The conjugate of claim 15, wherein the therapeutic drug is covalently attached to the dithiobenzyl moiety by a linkage selected from the group consisting of urethane, amine, amide, carbonate, thio-carbonate, ether and ester.

17. The conjugate of claim 15, wherein L is selected from the group consisting of cholesterol, a diacylglycerol, a phospholipid, and derivatives thereof.

18. The conjugate of claim 15, wherein L is a diacylglycerol to yield a conjugate having the structural formula:



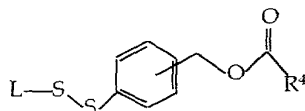
wherein R<sup>2</sup> and R<sup>3</sup> are hydrocarbons having between about 8 to about 24 carbon atoms.

19. The conjugate of claim 18, wherein R<sup>2</sup> and R<sup>3</sup> are hydrocarbons having from about 12 to about 22 carbon atoms.

20. The conjugate of claim 18, wherein R<sup>2</sup> and R<sup>3</sup> are hydrocarbon chains of the same length.

21. The conjugate of claim 15, wherein said drug is selected from the group consisting of mitomycin C, mitomycin A, bleomycin, doxorubicin, daunorubicin, fluorodeoxyuridine, iododeoxyuridine, etoposide, AZT, acyclovir, vidarabine, arabinosyl cytosine, pentostatin, quinidine, atropine, chlorambucil, methotrexate, mitoxantrone and 5-fluorouracil.

22. The conjugate of claim 15, wherein the therapeutic drug is covalently linked to the dithiobenzyl moiety to form a conjugate having the structure:



wherein R<sup>4</sup> represents a residue of the therapeutic drug.

23. The conjugate of claim 22, wherein R<sup>4</sup> is a therapeutic  
5 drug residue containing a primary or a secondary amine moiety  
thereby forming a urethane linkage between the dithiobenzyl and  
the therapeutic drug.

24. The conjugate of claim 23, wherein said therapeutic  
10 drug is selected from the group consisting of mitomycin A,  
mitomycin C, bleomycin and a polypeptide.

25. The conjugate of claim 22, wherein R<sup>4</sup> is a residue of  
15 a carboxyl-containing therapeutic drug, thereby to form an  
ester linkage between the dithiobenzyl and the therapeutic  
drug.

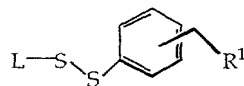
26. The conjugate of claim 25, wherein said drug is  
20 chlorambucil or methotrexate.

27. The conjugate of claim 22, wherein R<sup>4</sup> is a therapeutic  
drug residue containing a hydroxyl moiety thereby to form a  
carbonate linkage between the dithiobenzyl and the therapeutic  
drug.

28. The conjugate of claim 27, wherein the therapeutic  
25 drug is selected from the group consisting of  
fluorodeoxyuridine, iododeoxyuridine, etoposide, AZT,  
acyclovir, vidarabine, arabinosyl cytosine, pentostatin,  
30 quinidine, mitoxantrone and atropine.

29. A method for retaining a drug in a liposome,  
comprising  
preparing liposomes comprised of a vesicle-forming lipid

and of between about 1 to about 30 mole percent of a conjugate having the general form:



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wherein L is a hydrophobic moiety suitable for incorporation into a liposomal lipid bilayer, R<sup>1</sup> represents a therapeutic drug covalently attached to the dithiobenzyl moiety, and where orientation of the CH<sub>2</sub>R<sup>1</sup> group is selected from the ortho position and the para position,

whereby said preparing is effective to retain the drug in the liposomes until release from the conjugate in response to a physiologic condition or an artificially induced condition.

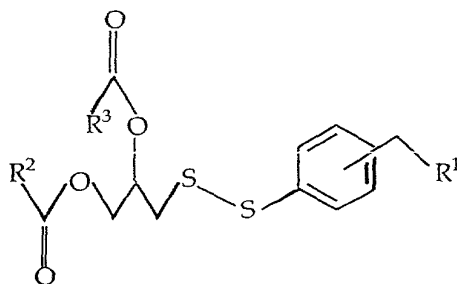
30. The method of claim 29, wherein said preparing includes preparing a conjugate where the therapeutic drug is covalently attached by a linkage selected from the group consisting of urethane, amine, amide, carbonate, thio-carbonate, ether and ester.

20

31. The method of claim 29, wherein said preparing includes preparing a conjugate wherein L is selected from the group consisting of cholesterol, a diacylglycerol, a phospholipid, and derivatives thereof.

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32. The method of claim 29, wherein said preparing includes preparing a conjugate wherein L is a diacylglycerol to yield a conjugate having the general structural formula:



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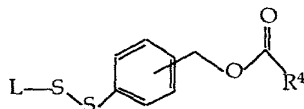
wherein  $R^2$  and  $R^3$  are hydrocarbons having between about 8 to about 24 carbon atoms.

33. The method of claim 18, wherein  $R^2$  and  $R^3$  are hydrocarbons having from about 12 to about 22 carbon atoms.

34. The conjugate of claim 32, wherein  $R^2$  and  $R^3$  are hydrocarbon chains of the same length.

35. The method of claim 29, wherein said preparing includes preparing a conjugate comprising a drug selected from the group consisting of mitomycin C, mitomycin A, bleomycin, doxorubicin, daunorubicin, fluorodeoxyuridine, iododeoxyuridine, etoposide, AZT, acyclovir, vidarabine, arabinosyl cytosine, pentostatin, quinidine, atropine, chlorambucil, methotrexate, mitoxantrone and 5-fluorouracil.

36. The method of claim 29, wherein said preparing includes preparing a conjugate comprising a therapeutic drug covalently linked to the dithiobenzyl moiety to form a conjugate having the structure:



wherein  $R^4$  represents a residue of the therapeutic drug.

37. The method of claim 36, wherein  $R^4$  is a therapeutic drug residue containing a primary or a secondary amine moiety thereby forming a urethane linkage between the dithiobenzyl and the therapeutic drug.

38. The method of claim 37, wherein said therapeutic drug is selected from the group consisting of mitomycin A, mitomycin C, bleomycin and a polypeptide.

39. The method of claim 36, wherein R<sup>4</sup> is a residue of a carboxyl-containing therapeutic drug, thereby to form an ester linkage between the dithiobenzyl and the therapeutic drug.

5        40. The method of claim 39, wherein said drug is chlorambucil or methotrexate.

10       41. The method of claim 36, wherein R<sup>4</sup> is a therapeutic drug residue containing a hydroxyl moiety thereby to form a carbonate linkage between the dithiobenzyl and the therapeutic drug.

15       42. The method of claim 41, wherein the therapeutic drug is selected from the group consisting of fluorodeoxyuridine, iododeoxyuridine, etoposide, AZT, acyclovir, vidarabine, arabinosyl cytosine, pentostatin, quinidine, mitoxantrone and atropine.